15:48:45 OCA PAD INITIATION - PROJECT HEADER INFORMATION 04/06/89

Active

Project #: E-16-A11 Cost share #: Rev #: 0
Center # : R6301-0A1 Center shr #: OCA file #:
Work type : RES
Contract#: CONT DTD 870317 Mod #: 4 Document : SUBCONT
Prime #: HL 15062 Contract entity: GTRC

Subprojects ? : N
Main project #:

Project unit: AE Unit code: 02.010.110
Project director(s):
GIDDENS D P AE (404)894-3781

Sponsor/division names: UNIV OF CHICAGO / CHICAGO, IL
Sponsor/division codes: 400 / 015

Award period: 861201 to 891130 (performance) 900131 (reports)

Sponsor amount	New this change	Total to date
Contract value	106,334.00	106,334.00
Funded	106,334.00	106,334.00
Cost sharing amount		0.00

Does subcontracting plan apply ?: N

Title: HEMODYNAMIC DETERMINANTS OF REGIONAL VULNERABILITY: NEAR WALL FLOW ...

PROJECT ADMINISTRATION DATA

OCA contact: Ina R. Lashley 894-4820

Sponsor technical contact

MR GODFREY S GETZ
(312)702-1265
DEPT OF PATHOLOGY,BH P617 (BOX 414)
5841 S MARYLAND AVE.,
CHICAGO IL 60637

Sponsor issuing office

JENNIFER RIEGELMANN
(312)702-9868
THE UNIVERSITY OF CHICAGO
970 EAST 58TH ST.,
CHICAGO IL 60637

Security class (U,C,S,TS) : U
Defense priority rating : N/A
Equipment title vests with: Sponsor GIT
NONE PROPOSED.

ONR resident rep. is ACO (Y/N): N
N/A supplemental sheet

Administrative comments -
MOD #4 IS A 1-YR EXTENSION OF E-25-655. ABOVE FUNDS ARE FOR THIS PERIOD ONLY.
TOTAL CUMULATIVE FUNDING UNDER THIS PROGRAM IS $ 333,433.

OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 05/04/90

Project No. E-16-A11 Center No. R6301-0A1

Project Director GIDDENS D P School/Lab AE

Sponsor UNIV OF CHICAGO/CHICAGO, IL

Contract/Grant No. CONT DTD 870317 Contract Entity GTRC

Prime Contract No. HL 15062

Title HEMODYNAMIC DETERMINANTS OF REGIONAL VULNERABILITY: NEAR WALL FLOW ...

Effective Completion Date 891130 (Performance) 900131 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	
Final Report of Inventions and/or Subcontracts	N	
Government Property Inventory & Related Certificate	N	
Classified Material Certificate	N	
Release and Assignment	N	
Other	N	

CommentsCONTINUED BY E-16-651. (CONTINUATION OF E-25-655).

Subproject Under Main Project No.

Continues Project No. E-25-655

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other	N
	N

July 16, 1989

SCOR ANNUAL PROGRESS REPORT - Part I Project B-1
(continuation application of HL 15062-19)

A. Narrative

1. Rationale of the project and relationship to SCOR program goals

Project B-1 is one of three closely related projects in Program B dealing with mechanical determinants of plaque formation and artery wall adaptation. Project B-1 focuses upon hemodynamic determinants of vulnerability to atherogenesis. The research is based upon the concept that the flux of atherogenic substances between the arterial wall and the bloodstream and the behavior of cells within the artery wall are influenced significantly by the local hemodynamic environment. This influence can be so strong that it may dictate whether atherosclerotic plaques will or will not develop at specific arterial sites.

This concept is explored by investigating the flow field, particularly phenomena occurring near the fluid-wall interface, using hemodynamic models of arteries susceptible to atherosclerosis and correlating the findings with a quantitative morphometric description of the distribution of atherosclerotic lesions in the arteries being modeled. Two models employed to date have been the human carotid bifurcation and the monkey aorta with coarctation, and particular attention is devoted to the wall shear stress created by the flowing viscous blood and to the residence time of blood-borne particles near specific sites along the arterial wall.

Information from Project B-1 is used as a basis for hypothesizing specific atherogenic mechanisms which can be studied collaboratively by the investigators of Program B and the cell and molecular biologists in Program A, using either in vitro, in vivo or in situ methods.

2. Summary of accomplishments during past year, including brief statement of Project's overall aims

The overall aims of Project B-1 are (i) to identify those hemodynamic factors that are closely correlated with the localization of atherosclerotic plaques in humans and in animal models of atherosclerosis; (ii) to employ these findings to hypothesize phenomena at the cellular and molecular levels which may be active in atherogenesis; and (iii) to collaborate with other investigators in Programs A and B to define experiments suitable for investigating these phenomena. To achieve these objectives it is necessary to perform specific hemodynamic model studies, to develop a new technique for tracking the trajectory of small particles in the modeled flow fields and to develop tools for computing flow field variables using the equations of fluid motion. It is hypothesized that the wall motion of an artery during the cardiac cycle and the non-Newtonian nature of blood may affect important details of near-wall flow behavior. These are, therefore, among the factors which are being investigated in Project B-1.

Plaque localization in the human carotid bifurcation has been shown to be closely correlated with the following fluid dynamic variables: (i) low mean wall shear stress (i.e., averaged over the pulsatile cycle); (i) low maximum wall shear stress (i.e., low values of the maximum of the stress during the cycle); and (iii) oscillations in wall shear stress direction during the pulsatile cycle. Further, during the past year we have shown, using qualitative

visualization of pulsatile flow with neutrally buoyant particles, that near-wall regions which develop plaques are also zones where (iv) the particle residence time is relatively long. These four variables all occur within the same region in the human carotid bifurcation, so that it cannot be determined which of these is more important by using this particular model.

Also during the past year, plaque localization in the aortas of monkeys which had moderate coarctations and were fed an atherogenic diet has been shown to correlate with low magnitudes of the instantaneous wall shear stress, regardless of direction. A better way of stating the correlation is that intimal thickening varies inversely with the maximum magnitude of wall shear stress, whether this magnitude results from forward or reverse directions of stress. We have not yet studied particle residence time in the coarctation model.

We have now completed several steps in the development of our particle tracking method. A new video system with dual cameras was purchased under National Science Foundation and Georgia Tech support, and the system has been made fully operational and interfaced with our MASSCOMP Data Acquisition System. Algorithms have been developed to identify particles in a flow field, outline the periphery of each particle, and calculate its centroid and video spatial coordinates. Algorithms to correct for the laboratory coordinate system and to identify the particle in a pair of biplanar images obtained with two cameras are nearing completion. This task has continued over the past two years because it requires the development of a new experimental technique in fluid dynamic measurements.

A compliant model of the human carotid bifurcation which has the identical geometry to that of a rigid model investigated previously has been developed, and laser Doppler anemometer studies of the velocity have begun. Results for wall shear stress measurements in the common carotid segment of the model show little effect of wall motion. This result is expected and gives a high level of confidence in our techniques for measuring wall shear in the presence of wall motion. We expect, based upon flow visualization studies with neutrally buoyant particles, to see larger effects of wall motion in the region of the carotid sinus as these experiments continue.

We have developed computer programs for solving the incompressible Navier-Stokes equations of fluid motion for three-dimensional geometries, and we have utilized sophisticated computer-aided graphics hardware and software to communicate our results. At present we are able to calculate the velocity field and wall shear stresses in curved tubes with variable area, including geometries yielding flow separation and reattachment. These techniques are being extended to bifurcation geometries and to pulsatile flows through axisymmetric configurations, such as the coarctation model. We are also examining the effects of non-Newtonian blood viscosity on flow separation and reattachment in a geometry with sudden expansion in an effort to assess the significance of non-Newtonian rheology on near-wall flow behavior. Preliminary studies in steady flow show that the location of flow reattachment, and consequently the size of the separation region, is foreshortened notably at low Reynolds numbers when a non-Newtonian model approximating blood rheology is employed.

The following present a brief summary of results obtained during the past year.

1. Wall shear stress measurements in the common carotid section of a compliant model of the human carotid bifurcation show little difference from those in a rigid model of the same geometry and flow conditions.

2. A qualitative assessment of flow visualization of neutrally buoyant particles in pulsatile flow through a rigid model of the human carotid bifurcation indicates that the region of the outer wall of the sinus, a region where plaques localize, has a relatively long particle residence time.
3. Qualitative assessment of flow visualization using neutrally buoyant particles in a compliant model of the human carotid bifurcation indicates that the flow in the sinus has somewhat more flow disturbance (i.e., larger flow separation, more complex secondary velocities) than for the case with the rigid model.

4. Intimal thickness in the poststenotic region of moderate coarctations in the aortas of cynomolgus monkeys fed an atherogenic diet correlates strongly with the reciprocal of the maximum magnitude of the instantaneous wall stress during the cycle regardless of stress direction. Correlation with the inverse of the mean wall shear stress was not as good. One suggestion arising from this result is that the arterial wall reacts to spare from lesion development if the local wall shear stress exceeds a critical value during the cardiac cycle. This may imply that it is the maximum stress rather than the mean value which is more important in plaque sparing. However, additional experiments are required before this can be concluded.

5. The size of the flow separation distal to a sudden expansion in a channel is reduced when a non-Newtonian model which approximates the steady state behavior of blood is employed in computations of the flow field. This may imply that the non-Newtonian nature of blood contributes in a protective way to reduce the extent of artery wall regions which experience flow reversal and low wall shear. Further studies are needed in this area.

3. Plans for the coming year

The development of our particle tracking technique will continue and will be applied to study particle velocity and residence time in models of the human carotid bifurcation and monkey coarctation.
The results will be correlated with intimal thickness measured in human and animal vessels.

Measurements of the velocity and wall shear stress in the compliant model of the human carotid will be completed, and the results will be used (i) to assess the significance of wall motion on the near-wall flow and (ii) to correlate with the distribution of human disease.

The effects of non-Newtonian rheology on near-wall flow variables will be studied using our computational fluid dynamics methods. Particular attention will be given to the effects on flow separation, reattachment, and wall shear stress distribution.

New experiments will be initiated to attempt to identify the separate effects of wall shear stress and particle residence time on atherogenesis as observed in an animal model. These experiments will be planned in collaboration with the other investigators of Program B and of Program A. A strong association of wall shear stress with atherogenesis suggests mechanisms related to the effects of physical forces on cell and molecular activity, while a strong association of particle residence time with atherogenesis suggests mechanisms related to mass transport and local availability of atherogenic substances.

C. Publications

1. B.B. Lieber, D.P. Giddens, R.I. Kitney and H. Talhami; "On the Discrimination Between Band-Limited Coherent and Random Apparent Stresses in Transitional Pulsatile Flow," Journaof Biomechanical Engineering, vol. III, pp. 42-46, February, 1989.

2. D. N. Ku, S. Glagov, J. Moore and C.K. Zarins; "Flow Patterns in the Abdominal Aorta Under Simulated Postprandial and Exercise Conditions: an Experimental Study," Journal of Vascular Surgery, Vol. 9, pg 309-316, February 1989.

3. A. Hamid K. MazHer and Don P. Giddens, "A Fast Algebraic Technique (FAT) to Generate 2D and 3D Grids for Arterial Flow Geometries," Journal of Biomechanical Engineering, accepted for publication.

4. A. Hamid K. MazHer and Don P. Giddens, "A Computational Approach to Blood Flow Through Arteries," Submitted to the Journal of Biomechanical Engineering.